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Quality and Safety

Fatal anaphylactic reaction to intravenous gadobutrol, a gadolinium-based MRI contrast agent

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ABSTRACT

We present the rare case of a fatal anaphylactic reaction to gadobutrol, a magnetic resonance imaging contrast agent, in a 42-year-old man. The patient underwent elective magnetic resonance imaging for diagnostic clarification of a suspicious finding in the abdomen. The patient had undergone contrast-enhanced computed tomography previously without the occurrence of any adverse effects. Adverse drug reactions in gadobutrol have a very low prevalence of 0.32%-3.5%, with serious adverse drug reactions in <0.1%. There are only a few cases of fatal anaphylactoid reactions to gadolinium-based contrast agents in general. However, if an anaphylactoid reaction occurs, it can present itself with a fulminant course within minutes.

Case history

A 42-year-old man underwent elective magnetic resonance imaging (MRI) for diagnostic clarification of a suspicious finding in the abdomen. The patient had undergone contrast-enhanced computed tomography previously without the occurrence of any adverse effects.

A few minutes after the application of the MRI contrast agent Gadovist (active substance: gadobutrol), the patient pressed the alarm button complaining first about nausea, then also dyspnea. With the suspected diagnosis of an allergic reaction, the patient was administered an ampoule of the antihistamine Tavegyl (2 mg/2 mL, active substance: clemastine), the H2-receptor-antagonist Zantic (50 mg/5 mL, active substance: ranitidine), and the glucocorticoid Fortecortin (40 mg/5 mL, active substance: dexamethasone) intravenously. The patient developed cold sweat, his pulse was hardly any more palpable, and he lost consciousness. Defibrillation pads were placed, the heart frequency was analyzed, and cardiac massage had to be started. With progressive swelling of the airways, the patient also had to be intubated. Resuscitation was performed for approximately 1 hour during which time the patient was transferred to the university hospital. The patient was then hemodynamically stable but sedated

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Written informed consent for the case to be published (including images, case history, and data) was obtained from the responsible public prosecutor's office for the publication of this case report, including accompanying images.

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Fig. 1 – Computed tomography (axial view) of the edematous brain, 1 day after the incident.

and ventilated. In the blood samples obtained upon admission to the hospital, the enzyme tryptase was considerably elevated (>200 µg/L, normal <11.4 µg/L).

Therapy with antihistamines and steroids was continued. The patient's body was kept at a maximum of 36°C (96.8°F) to prevent further brain damage. Yet, cranial computed tomography 1 day later showed a reduced differentiation of the brain cortex and the medulla, missing contrast of the basal ganglia and general brain edema as a result of severe lack of oxygen (Fig. 1). With an overall poor prognosis and in consultation with the relatives, it was decided to stop all intensive care treatments. The patient died 2 days later.

Autopsy

Autopsy showed massive brain edema (1450 g, Fig. 2), venous congestion, and mild thorax trauma due to the resuscitation measurements (rib fractures and subcutaneous hemorrhage near the sternum). Besides massive brain edema, no other findings causative of death could be found. The cause of death was therefore determined to be paralysis of the respiratory system due to brain edema following lack of oxygen during long-lasting resuscitation measurements in consequence to the anaphylactic reaction to the MRI contrast agent Gadovist.

Discussion

There are several gadolinium-based contrast agents for contrast-enhanced MRI that are approved for clinical use. Consisting of a paramagnetic metal, they increase signal intensity and thereby tissue contrast in MRI. The contrast agent administered in the present case was gadobutrol (Gadovist; Bayer Schering Pharma AG, Berlin, Germany), a highly stable, non-ionic, macrocyclic gadolinium MRI contrast agent that was first introduced in Switzerland in 1998 [1]. Gadobutrol distributes rapidly into the extracellular space and is eliminated by glomerular filtration [2]. Gadobutrol has been placed in the lowest-risk category for the development of nephrogenic systemic fibrosis in patients with renal impairment [1,3]. Adverse drug reactions (ADRs) for gadobutrol were reported in 0.32%-3.8% [1,2,4,5], mostly in terms of nausea, vomiting, urticaria, and dizziness, with serious ADRs in <0.1% [1,2,4,5]. The onset of ADRs occurred within 5 minutes in 62% [2] to 82.4% [4] of the patients. Most of the rest of the ADRs occurred within 15 [4] to 24 hours [2]. In the electronic database FDA Adverse Event Reporting System of the United States, there are 614 cases reported of ADRs to gadolinium-based contrast agents in general (1998-2012), of which 7.2% had a fatal outcome [6].

Conclusion

Anaphylactic reaction to an MRI contrast agent is a very rare complication [6,7] but can have a relentless course within minutes when it occurs. Even in a medical setting with highly trained professionals, the outcome can be fatal. Therefore, on the one hand, it is important for clinicians to know that even

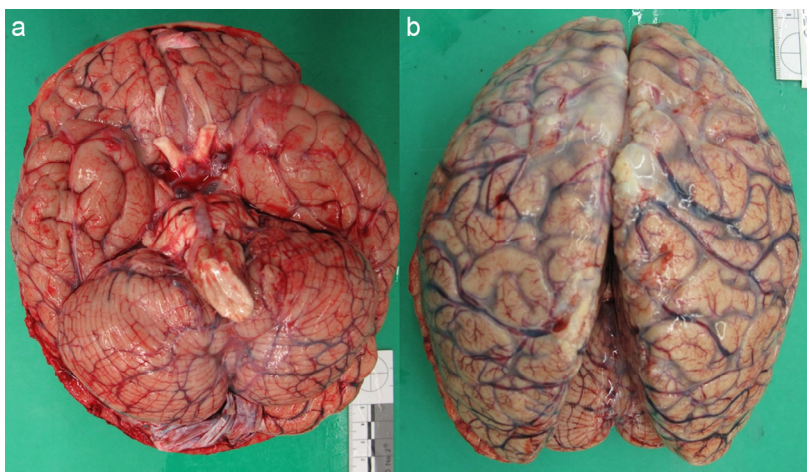

Fig. 2 – Photography of the edematous brain (1450 g) at autopsy. (A) Caudal view. (B) Cranial view.

at MRI examinations, fatal accidents can occur quite suddenly and to make sure resuscitation equipment as well as well-trained staff is available all the time [8]. Forensic pathologists, on the other hand, have to be aware of those rare causes of fatal anaphylactic reactions while investigating sudden death after medical treatments or examinations.

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